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Complete lignocellulose conversion with integrated catalyst recycling yielding valuable aromatics and fuels

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Lignocellulose, the main component of agricultural and forestry waste, harbours tremendous potential as a renewable starting material for future biorefinery practices. However, this potential remains largely unexploited due to the lack of strategies that derive substantial value from its main constituents. Here, we present a catalytic strategy that is able to transform lignocellulose to a range of attractive products. At the centre of our approach is the flexible use of a non-precious metal catalyst in two distinct stages of a lignocellulose conversion process that enables integrated catalyst recycling through full conversion of all process residues. From the lignin, pharmaceutical and polymer building blocks are obtained. Notably, among these pathways are systematic chemo-catalytic methodologies to yield amines from lignin. The (hemi)cellulose-derived aliphatic alcohols are transformed to alkanes, achieving excellent total carbon utilization. This work will inspire the development of fully sustainable and economically viable biorefineries.

Lignocellulose is a non-edible, renewable starting material consisting of lignin, cellulose and hemicellulose, which harbours significant potential for the sustainable production of chemicals and fuels[1,2]. Yet, unlocking this potential requires fundamentally new catalytic methods[3] and innovative biorefinery approaches that are able to accommodate the structural complexity of lignocellulose and derive value from all its major components.[4]

In a typical biorefinery, lignocellulose is first separated to its constituents by pre-treatment[2]. This approach, however, is energy intensive, and predominantly focuses on producing high-quality cellulose[4]. Moreover, under these processing conditions the lignin component is structurally modified, rendering its further catalytic valorization very challenging[4–7]. This remains true despite impressive advances in the selective conversion of lignin model compounds[8,9] and depolymerization of organosolv lignin[10–14]. Recently, elegant research has focused on lignocellulose fractionation in the presence of a catalyst[4,15–17]. While these methods hold much promise for the selective production of aromatic monomers from the lignin fraction, they leave a significant portion of the renewable carbon equivalents unutilized and mixed with the catalyst. Thus, in these systems it is (mainly) the cellulose part that is tedious to valorize and catalyst recycling has been identified as a key challenge[4,16].

To enable efficient catalyst recycling and achieve the valorization of all lignocellulose constituents without pretreatment, we devised a strategy that takes advantage of the special reactivity of a copper-doped porous metal-oxide catalyst in supercritical methanol[18]. When this non-noble-metal catalyst was applied in a two-step manner during catalytic lignocellulose fractionation, the lignin fraction was converted to aromatics in high selectivity, and the cellulose-rich solid residues were fully transformed to aliphatic small molecules, liberating the catalyst for re-use and offering a distinct advantage over existing systems[4]. Importantly, this approach delivers aromatic and aliphatic alcohols from lignocellulose, which retain part of the functionality inherent to the renewable starting material and are thus ideally suited substrates for accomplishing direct, atom-economic transformations toward products with concrete valorization potential. Notably, among these pathways are systematic methodologies to obtain lignin-derived amines, including the highly challenging direct coupling with ammonia[19,20], producing water as the only by-product. The overall strategy seeks to maximize sustainability in the individual reaction steps and globally through minimizing the number of reaction steps required and significantly reducing the amount of waste formed. The unique balance between cleavage and coupling pathways allows access to chemical diversity in products, which is necessary to achieve competitiveness with current fossil-fuel-based pathways.

Results

Catalytic strategy. The global catalytic strategy established here consists of three stages (Fig. 1) in which lignocellulose is fully converted, yielding a range of valuable products without any energy-intensive pretreatment. At the core of this approach is the flexible use of a non-noble-metal catalyst, copper-doped porous metal oxide (Cu20-PMO)[18], in two distinct steps (Step 1 and Step 2) of this lignocellulose conversion process (LignoFlex). Through mild reductive treatment an aromatic alcohol is obtained with high selectivity (Stage 1, Step 1). Next, all process residues containing unreacted (hemi)cellulose and lignin are fully converted to aliphatic small molecules, taking advantage of the unique reactivity of the Cu20-PMO in supercritical methanol[18] (Stage 1, Step 2). Thereby, the catalyst can be readily recycled. An advanced network of transformations was designed for the catalytic transformation of the obtained alcohols (Fig. 1, Stage 2–3). These include the divergent functionalization of the lignin-derived aromatic alcohol to a small

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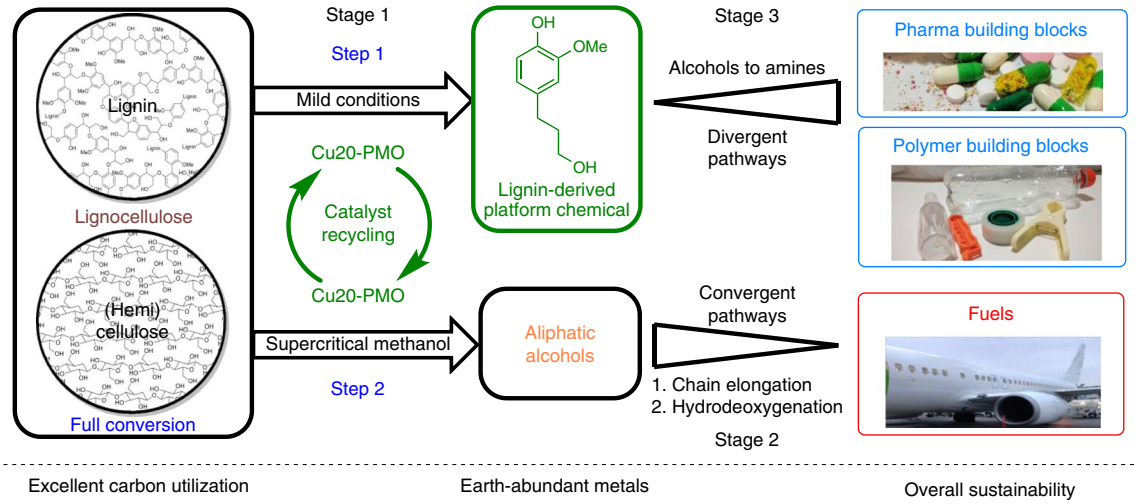


Fig. 1 | Comprehensive catalytic strategy for complete lignocellulose conversion, which embraces the inherent complexity of the starting material. Lignocellulose is used without pre-treatment and is fully converted to a range of attractive products. Stage 1: the flexible application of a Cu20-PMO catalyst to produce aromatic (Step 1) and aliphatic (Step 2) alcohols with integrated catalyst recycling (LignoFlex). Stage 2: convergent pathways for the conversion of the aliphatic alcohols obtained from the unreacted lignocellulose residues to clean mixtures of alkanes through chain elongation and hydrodeoxygenation (HDO). Stage 3: divergent functionalization of a lignin-derived platform chemical to a range of value-added building blocks via direct, atom-economic pathways.

library of value-added compounds that can serve as pharmaceutical or polymer building blocks. Focus is devoted to straightforward and atom-economic pathways that permit rapid conversion of the lignin-derived platform chemical to higher-value products that can enter the chemical supply chain at a much later stage than bulk chemicals derived from petroleum.

Secondly, convergent catalytic transformation of complex mixtures of cellulose-derived aliphatic alcohols to fuel-range alkanes via chain elongation[21] and hydrodeoxygenation (HDO) results in clean mixtures of alkanes. These strategies are described in detail in the appropriate sections of the manuscript.

Aromatic monomers from lignocellulose. To obtain aromatics directly from lignocellulose (Stage 1, Step 1), we started our investigations by treating pine lignocellulose over a Cu20-PMO catalyst (Supplementary Methods Section 3) in a reductive atmosphere at 140–220 °C. The results are summarized in Fig. 2a and Table 1. The products consisted of a clear, colourless methanol solution and a solid residue containing unreacted lignocellulose and catalyst, which was further treated as described below. To our surprise, at 180 °C, the small molecule fraction of the liquid phase contained predominantly one aromatic compound, dihydroconiferyl alcohol (**1G**), which could be isolated. Earlier studies using noble-metal catalysts and higher temperatures reported **2G** as the main product in mixtures, and **1G** was also seen before[16]. Remarkably, in our system **1G** was obtained in excellent (>90%) selectivity (Fig. 3b) with a non-noble-metal catalyst under relatively mild conditions (180 °C). The higher degree of functionality in **1G** provides an excellent handle for further modifications, as described in Stage 3 below.

The above results can be explained by the selective depolymerization of lignin that is released from the lignocellulose matrix (Fig. 2b). Based on model compound studies (Supplementary Note 2) we propose that depolymerization proceeds via scission of the β-O-4 linkage through a series of dehydrogenation, hydrogenolysis and hydrogenation events involving a ketone intermediate[22]. This is in agreement with existing two-step methods that achieve efficient depolymerization of organosolv lignin to aromatics through selective pre-oxidation followed by reductive cleavage[10,12]. In the present study, this sequence of steps occurs over a single, multifunctional catalyst, providing **1G** in superior selectivity.

To demonstrate the clear advantage of the applied catalytic conditions, control reactions were performed (Supplementary Note 3). Indeed, while the 2D NMR spectrum of a sample obtained on standard catalytic treatment (Cu20-PMO and H_2) was assigned to the main product **1G** (Fig. 3a,b), a control reaction using pine lignocellulose only delivered a brown solution of organosolv lignin, as evidenced by 2D NMR analysis that showed all relevant lignin linkages intact (Fig. 3c). Thus, in this case, lignin was extracted from the lignocellulose substrate but was not depolymerized in the absence of catalyst. This was also confirmed by comparing the gel permeation chromatography (GPC) traces of a control and a catalysed reaction (Fig. 3d). Further, pre-extracted organosolv lignin underwent depolymerization under standard catalytic conditions (Fig. 3e), but resulted in lower monomer yield (Table 1, entry 6) and more oligomers. This is due to the modification of the native lignin structure during organosolv processing resulting in fewer cleavable β-O-4 linkages[5] and underscores the advantage of using lignocellulose as substrate directly.

The flexible use of Cu20-PMO for full material utilization. After obtaining **1G** from pine lignocellulose in excellent selectivity, the generality of the approach was demonstrated using a variety of wood types (Fig. 4, Table 2 and Supplementary Table 2) and catalyst recycling was integrated (Stage 1, Steps 1 and 2). High aromatic monomer yields were achieved in most cases, especially with poplar (36%), beech (31%) and maple (30%) lignocellulose. Interestingly, all product mixtures contained typically two, and a maximum of three main products, the type of which depended on the native structure of each lignin. We found alcohol **1S** as the main product when starting from poplar, beech or maple lignocellulose. Predominantly **2S** was obtained from oak and mainly **1G** from pine and cedar lignocellulose. Interestingly, we were able to isolate both **1G** as well as **1S** as pure compounds from a run with maple wood (Supplementary Table 2, entry 6). A good correlation was observed between the syringyl/guaiacyl (S/G) ratio measured in the starting lignin and the S/G ratio of the corresponding aromatic products (Supplementary Table 4).

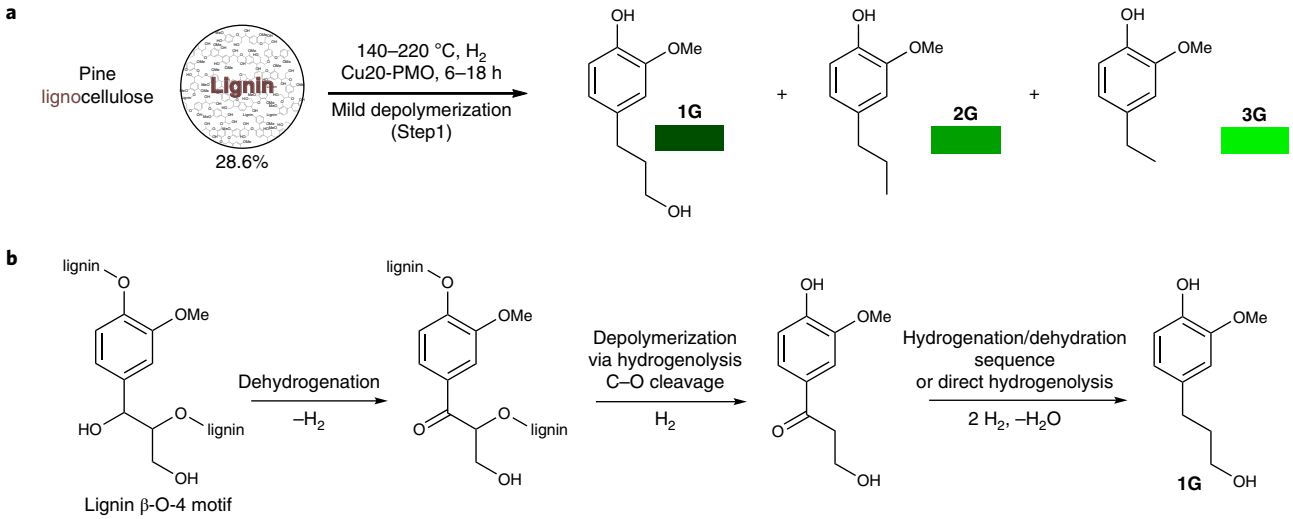


Fig. 2 | Aromatic monomers from pine lignocellulose. a, Reductive treatment of pine lignocellulose over copper-doped porous metal oxide (Cu20-PMO) resulting in the formation of one aromatic monomer, dihydroconiferyl alcohol (**1G**), in high selectivity. (For identification of lignin depolymerization products see Supplementary Figs. 1 and 2). **b**, Proposed reaction steps during selective lignin depolymerization via cleavage of the most-abundant β-O-4 linkage (Supplementary Note 2).

Table 1 | Monomer yields depending on experimental conditions

Entry[a]	1	2	3	4[b]	5[c]	6[d]
Temperature (°C)	180	140	220	180	180	180
Substrate (g)	1	1	1	1	2	0.2
Monomers (mg)[e]	29	4	36	18	48 (40)	8
Monomer yield (%)[f]	10	1	13	6	9 (7)	4
Monomer distribution	4% 10% 86%	100%	6% 33% 61%	11% 89%	8% 92%	12% 25% 63%

For more details see Supplementary Table 1 and for a product formation profile see Supplementary Fig. 3. [a]General conditions: 0.2 g Cu20-PMO, $t = 18$ h, 10 ml methanol, 40 bar H_2. [b]$t = 6$ h. [c]0.4 g Cu20-PMO. [d]Using pre-extracted pine organosolv lignin as substrate. [e]Based on gas chromatography–flame ionization detection (GC-FID) (calibrated). Number in brackets shows isolated yield of **1G**. [f]Monomer yield = $\text{weight}_{\text{monomers}}$ / $\text{weight}_{\text{lignin}}$.

In contrast to typical depolymerization procedures, which generally result in complex product mixtures[6,7], the great advantage of the mild and selective catalytic method developed here is that only a few aromatic compounds are obtained and single products can be easily separated. Undesired side reactions, such as overreduction of the aromatic rings[6,7] or recondensation of reactive fragments[23] formed during lignin depolymerization, are minimized under these conditions. However, this method leaves linkages other than the β-O-4 intact, thus a fraction of lignin is unconverted. Additionally, the whole of the (hemi)cellulose portion (~60% by mass), which makes up a significant quantity of renewable carbon equivalents, remains unutilized. These solid residues stay mixed with the heterogeneous Cu20-PMO, making catalyst recycling very challenging. To overcome this challenge, we envisioned liberating the catalyst through conversion of the solid residues to valuable products. This catalyst-recycling step relies on the unique reactivity of Cu20-PMO in supercritical methanol at 300–320 °C, whereby a fraction of the solvent undergoes in situ methanol reforming to create reaction conditions suitable for the complete conversion of lignocellulose to small molecules[21]. We anticipated that the unreacted solid residues formed in Step 1 could also be converted, assuming that no catalyst deactivation took place during this initial processing step. Indeed, excellent conversion of the reaction solids was achieved by simply heating the residues from runs **M1**–**M8** to 320 °C in freshly added methanol (Table 2, Supplementary Table 7).

The composition of the obtained clear, colourless methanol solutions (**SMix1**–**SMix8**) was largely similar irrespective of the starting material (all containing mainly cellulose), with slight differences originating from the lignin structure of the original wood samples. These mixtures consisted predominantly of aliphatic alcohols, small amounts of ethers and esters, as well as minor amounts of alkyl-phenols (Supplementary Figs. 4–12 and Supplementary Tables 6 and 7).

Recycling experiments comprising both Step 1 and Step 2 were carried out using pine lignocellulose to obtain aromatic and aliphatic alcohols, respectively (Supplementary Tables 13 and 14, and Supplementary Note 4). Characterization of the catalyst after the first such cycle showed regularly distributed Cu nanoparticles of 20–50 nm, characteristic for an active catalyst (Supplementary Note 1 and Supplementary Fig. 78b). Indeed, full lignocellulose conversion was maintained for a total of 10 runs (5 mild, 5 supercritical). A small decrease in **1G** yield in the fifth mild run and a change in product composition in the fifth supercritical run was observed and accordingly, aggregation of magnesium and copper was observed after a total of 10 runs (Supplementary Fig. 78).

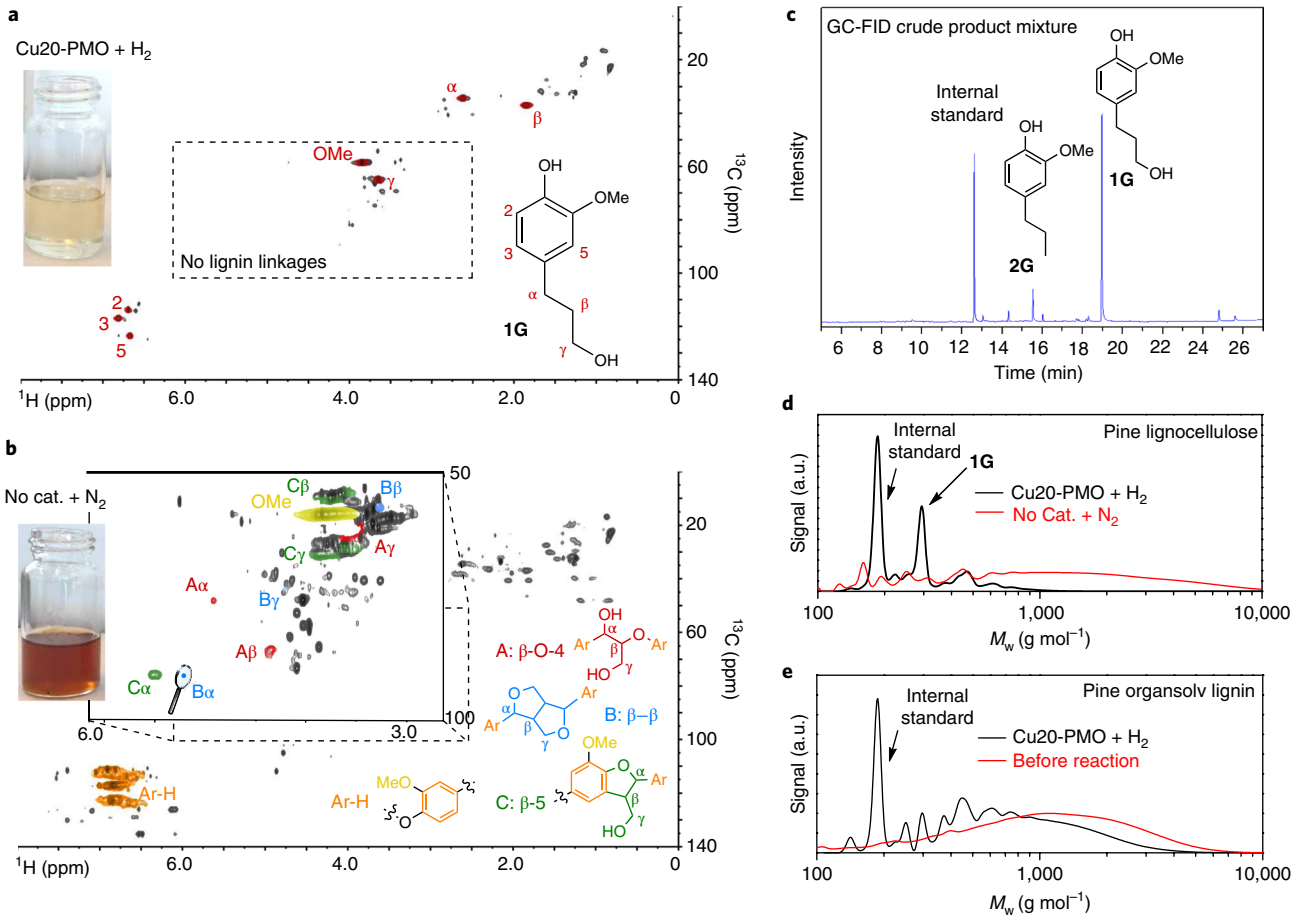


Fig. 3 | Catalytic and control reactions for the conversion of pine lignocellulose. a, 2D NMR spectrum of a catalysed reaction (1 g lignocellulose, 0.2 g Cu20-PMO, 40 bar H_2, 10 ml methanol, 18 h). The signals are clearly assigned to **1G**. **b**, 2D NMR spectrum of a control reaction using lignocellulose but no catalyst (1 g lignocellulose, 40 bar N_2, 10 ml methanol, 18 h). Characteristic signals of the main lignin linkages are marked red (β-O-4), blue (β-β) and green (β-5). A spectrum typical for an organosolv lignin is seen in which all relevant lignin linkages are intact. **c**, GC-FID trace of the crude product on mild reductive treatment of lignocellulose (Table 1, entry 5) showing the formation of **1G** in excellent selectivity. **d**, Gel permeation chromatograms (GPC) of products when lignocellulose was used as substrate. Black: catalysed reaction, showing efficient depolymerization. Red: control reaction confirming the lack of depolymerization. **e**, GPC traces. Black: organosolv lignin after catalytic treatment (Table 1, entry 6) showing depolymerization, but increased amount of oligomers compared with lignocellulose as substrate. Red: pre-extracted pine organosolv lignin before reaction. (For extraction of organosolv lignin see Supplementary Method Section 5 and Supplementary Table 3.)

Elemental analysis of the liquid samples after the first and the fourth mild and supercritical runs showed minimal leaching of Cu, Mg or Al (Supplementary Table 15).

Catalytic conversion of the aliphatic alcohols to fuel-range alkanes. We further focused on catalytic conversion of the product mixture **SMix1** obtained after the treatment of pine lignocellulose residues in supercritical methanol (Stage 2). The major components contained in **SMix1** were aliphatic alcohols with a chain length of C2–C5, many of them isomers. Thus, we envisioned a convergent strategy towards alkanes that can serve as liquid transportation fuels (Fig. 5a). This involved chain elongation first, and subsequent exhaustive HDO to increase selectivity in the product alkanes. To increase the chain length of the alcohols, a suitable biomass-derived building block was necessary. Elegant studies have shown the palladium-catalysed alkylation of acetone with aliphatic alcohols[24,25]. Bio-derived furfural[26] and cyclopentanone[27] were previously used in diverse coupling reactions to produce diesel-range alkanes on HDO. Inspired by these studies, we developed a new chain-elongation methodology (Fig. 5b) for the coupling of cyclopentanone with 1-pentanol (as model for **SMix1**, Supplementary Note 5) using a CuNi-PMO that was previously designed in our laboratory[28]. A model mixture consisting of 10 different alcohols was also successfully converted (Supplementary Note 6).

Next, the considerably more-complex **SMix1** was used directly (Supplementary Note 7), however the presence of methanol hampered reactivity. On solvent exchange to heptane (Supplementary Fig. 84), the desired coupling reaction could be readily performed under optimized reaction conditions. It is remarkable that a complex alcohol mixture **SMix1** resulted in a relatively easy-to-analyse mixture of cyclic ketones (Supplementary Fig. 86), which on successful HDO over a commercially available Ni/SiO_2-Al_2O_3 catalyst delivered clean mixtures of alkanes, which were quantified (Supplementary Table 18). The products fell into two main categories: C4–C6 alkanes originating from branched or cyclic uncoupled alcohols, and transportation fuel range, C8–C11, alkanes from the coupling of cyclopentanone with aliphatic alcohols in **SMix1** and of lignin-derived propyl-cyclohexanols.

Reaction network towards value-added aromatics. Approaches that take advantage of the inherent complexity of renewable starting materials, instead of markedly reducing it, hold the potential of developing fully sustainable processes, especially when products of

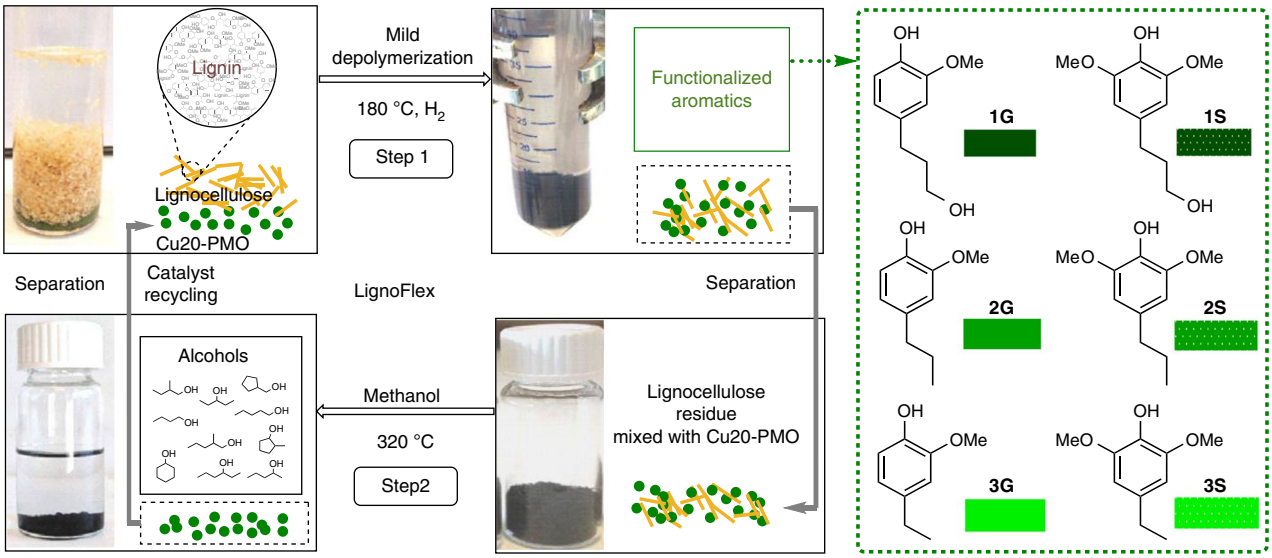


Fig. 4 | Complete conversion of various lignocelluloses to aromatic and aliphatic alcohols through the flexible use of Cu20-PMO under mild (Step 1) and supercritical conditions (Step 2). Process steps including catalyst recycling. Step 1: aromatic monomers obtained on mild treatment. Step 2: conversion of solid residues using Cu20-PMO in supercritical methanol, and selectivities of compound groups obtained. (For lignin content determination of each lignocellulose see Supplementary Table 5.)

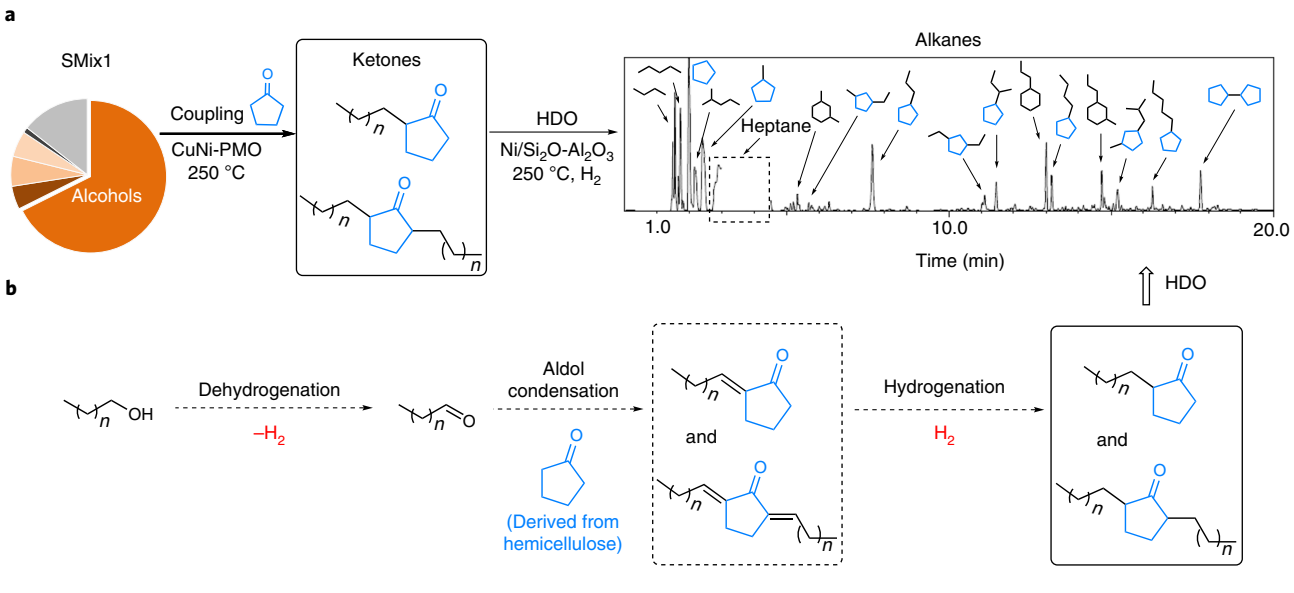
Table 2 | Results on full conversion of various types of lignocellulose

	Pine	Walnut	Poplar	Oak	Beech	Maple	Alder	Cedar
Step 1								
Monomers (mg)[a]	29	48	67	51	59	79[d]	45	36
Monomer yield (%)[b]	10	9	36	17	31	30	20	10
Monomer distribution	86%	31%	42%	53%	59%	52%	38%	67%
	M1	M2	M3	M4	M5	M6	M7	M8
Step 2								
Conversion (%)[c]	100	92	100	96	100	100	100	97
Selectivity	68%	61%	61%	53%	61%	57%	60%	52%
	SMix1	SMix2	SMix3	SMix4	SMix5	SMix6	SMix7	SMix8

Step 1 conditions: 0.2 g Cu20-PMO, 1 g lignocellulose, 10 ml methanol, 180 °C, 40 bar H_2, 18 h. Step 2 conditions: 12 ml methanol, 320 °C, 6 h. [a]Calculated based on GC-FID (calibrated). [b]Monomer yield = $\text{weight}_{\text{monomers}}$ / $\text{weight}_{\text{lignin}}$. [c]Conversion based on the weight of the remaining solid residue. [d]Isolated yield of **1G** (22 mg), **1S** (31 mg).

higher value are desired (Fig. 6a). In this respect, **1G** can be easily isolated as pure compound and subsequently transformed to a set of value-added products (Stage 3; Fig. 6 and Supplementary Fig. 13). Mild depolymerization strategies result in intermediates that maintain important functionality, which allows straightforward conversion to higher-value products. Such pathways are direct and atom-economic and lead to value-added chemicals with minimal waste and energy input. The obtained compounds would enter the chemical supply chain at a higher level of functionality than bulk chemicals derived from petroleum, ensuring competiveness with fossil-derived pathways. This offsets the need for multiple functionalization steps developed for petroleum-derived simple building blocks via classical pathways that are associated with the production of copious amounts of waste. Regarding lignin valorization, such an approach is a viable alternative to strategies that attempt to convert lignin into chemicals of very low functionality, in particular when products containing heteroatoms are desired (see example shown in Supplementary Fig. 14).

First, we focused on functionalization on the aliphatic alcohol moiety in **1G** (Fig. 6b). Amines play a central role in the chemical industry since nitrogen-containing compounds are key structural motifs in pharmaceutically active compounds, polymers or surfactants[19,20]. Surprisingly however, systematic chemo-catalytic approaches for the production of amines from lignin[29] have, to the best of our knowledge, not been realized. The shortest and highly atom-economic route towards bio-based amines is the direct coupling of lignin-derived alcohols with ammonia, producing water as the only by-product. However, only a few homogeneous and heterogeneous catalytic methods are known to yield amines[30,31] or nitriles[32] from alcohols



c

Carbon weight of starting materials (mg)		Carbon weight of products (mg)									Yield based on carbon content	
		Alkanes										
Pine solid residue	Cyclopentanone		C4	C5	C6	C8	C9	C10	C11+	Total alkanes	C8+ alkanes	A	B
368	68	Heptane soluble	28	99	31	18	13	19	9	217	60	54%	45%
		Heptane insoluble	3	4	1	5	1	1	2	18	9		

Fig. 5 | Catalytic methodology for the conversion of lignocellulose-derived alcohols to alkanes. a, The major fraction of the aliphatic small molecules obtained on conversion of the pine lignocellulose residues (**SMix1**) are aliphatic alcohols. These alcohols undergo chain elongation through coupling with cyclopentanone to yield a mixture of ketones (CuNi-PMO, heptane) followed by HDO (Ni/SiO_2-Al_2O_3, 40 bar H_2) to clean mixtures of (predominantly) cyclic alkanes. A representative gas chromatography–mass spectrometry (GC-MS) trace of the crude product mixture is shown in Supplementary Fig. 89. **b**, Proposed reaction sequence during the chain elongation reaction promoted by a CuNi-PMO possessing sufficient dehydrogenation activity and appropriate surface basicity. **c**, Carbon weights of starting material and alkane products as well as total carbon yields (see Supplementary Note 9 for details of calculation). Cyclopentanone present, yield A = total alkanes / (pine solid residue + cyclopentanone); No cyclopentanone present, yield B = (total alkanes – cyclopentanone) / pine solid residue. For details on solvent exchange see Supplementary Methods Section 11 and related reactions see Supplementary Notes 5–8. For quantification see Supplementary Table 18. The HDO catalyst shows excellent robustness (Supplementary Fig. 87).

directly and the efficiency of these is largely limited by the structure of the substrate. We have found that a versatile building block, nitrile **4**, can be obtained through direct transformation of **1G** with ammonia using commercially available Ni/SiO_2-Al_2O_3. The reaction proceeds through a series of dehydrogenation events via the corresponding aldehyde and imine intermediates (Supplementary Note 10). Hydrogenation of **4** under mild reaction conditions provided **5** in analytical purity. Reductive defunctionalization of **1G** resulted in the formation of **3G** in high selectivity. Hydrolysis of **4** led to the corresponding dihydroferulic acid **6**, which was in one step catalytically[33] converted to styrene derivative **7** in a good (72 %) isolated yield. This is a high yielding route to a functionalized styrene from lignin or lignocellulose. Both **6** and **7** can serve as valuable building blocks for polymer synthesis, as detailed further below.

Next, we established the direct conversion of **3G** to aniline derivatives (Fig. 6c) through homogeneous nickel-catalysed cross-coupling[34,35] using a variety of amines and pseudohalogenide **8** that was obtained from **3G**. Gratifyingly, **8** underwent cross-coupling with a number of amines to yield the corresponding aromatic products **9a**–**9e**. Nonetheless, the inherent structure of lignin-derived **3G** also posed limitations to the methodology applied, since in many cases no reactivity was observed or there was a competing side reaction (Supplementary Table 8). Interestingly however, quantitative deoxygenation[36] of **8** delivered 3-ethylanisole (**10**), which cannot be obtained by electrophilic aromatic substitution of anisole, presenting a distinct advantage of using a lignin-derived substrate.

Finally, a phenol-to-aniline transformation[37] (Fig. 6d) was carried out through oxidation of **1G** to the corresponding benzoquinone ketal **11** and a subsequent reaction with glycine methyl ester hydrochloride to provide the desired aniline, **12a**. The inherent structure of **1G** was largely beneficial for obtaining excellent yields of **12a**, since the 3-hydroxy moiety was ideally positioned to obtain **11**, a stable spiro-compound[38]. The corresponding one-pot procedure was applied to **3G**, yielding aniline derivative **12b**. Finally, **13**, an *N*-mesyl derivative, was prepared from **1G** by direct amination of the aliphatic alcohol moiety through a hydrogen borrowing strategy[39]. Subsequently, **13** was converted to the aliphatic–aromatic diamine **12c**.

Beside the network established with guaiacol-type monomers, we have also successfully performed selected transformations involving syringol-type monomers, summarized in Supplementary Note 12.

Summary and future outlook. The central aim of our established catalytic strategies is to achieve full conversion of lignocellulose without the separation of its main components and to obtain products that find value in a variety of applications (Fig. 7). Besides the fuel-range alkanes obtained from the (hemi)cellulose fraction, the single aromatic compounds that were obtained here in sufficient yield and proper functionality from lignin may serve as value-added starting materials (Fig. 8) for various applications.

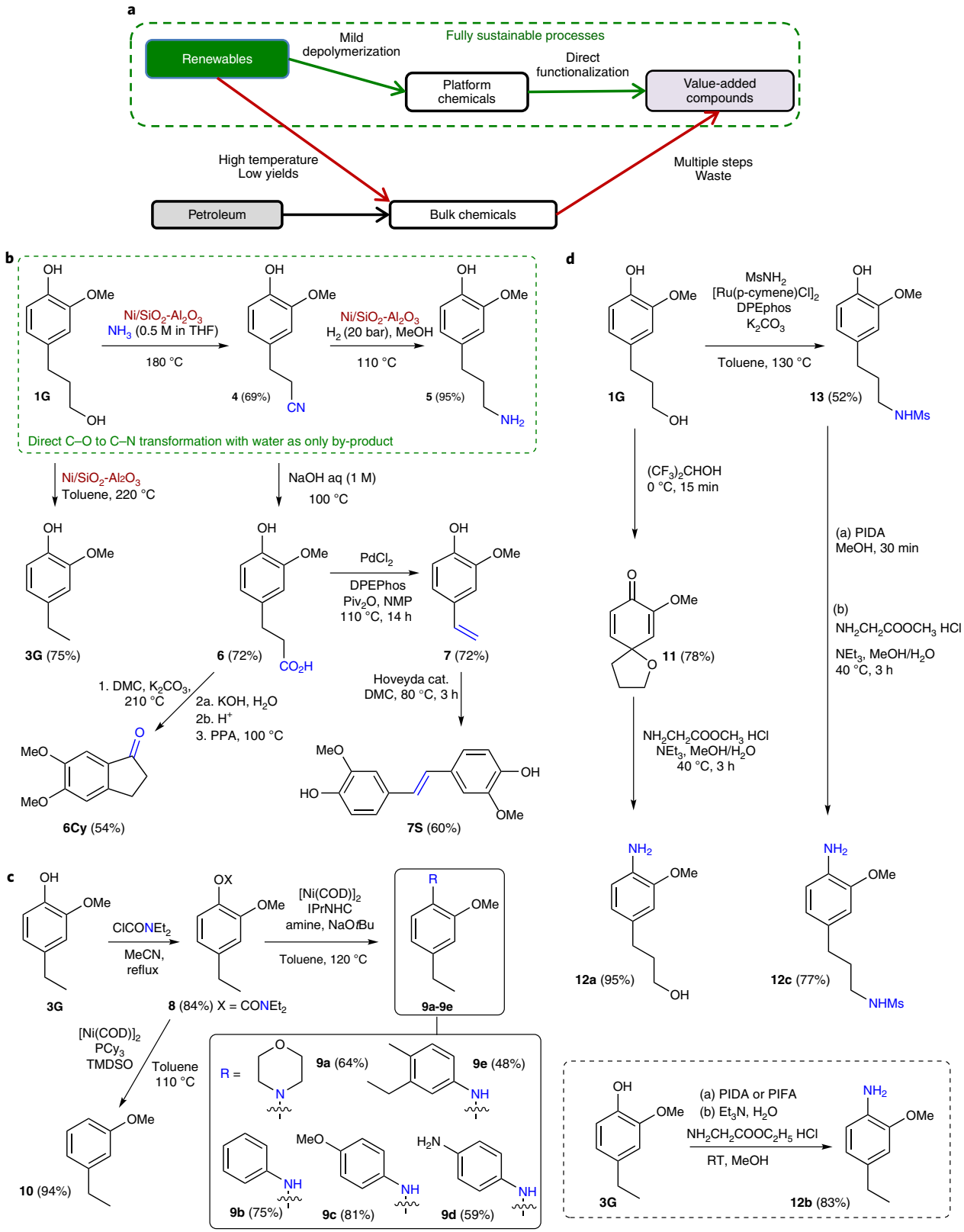


Fig. 6 | Toward fully sustainable processes. a, The ultimate aim is to develop fully sustainable processes through mild and selective catalytic conversion of renewables (lignin) to platform chemicals (such as **1G**). **b**–**d**, The conversion of lignin-derived platform chemical **1G** to a range of value-added compounds, including aromatic amines. **b**, Direct functionalization of the aliphatic alcohol moiety of **1G**. **c**, Homogeneous Ni-catalysed cross coupling of **8** with various amines and defunctionalization. **d**, High-yield phenol to aniline transformations using **1G** and its derivatives (see Supplementary Methods Section 12 for related experimental details). Selected reactions were also performed with **1S** and **3S** (Supplementary Note 12). The reaction network was established using commercially available **1G**. Selected pathways over multiple steps were also performed starting from **1G** isolated from lignocellulose (Supplementary Notes 10 and 11).

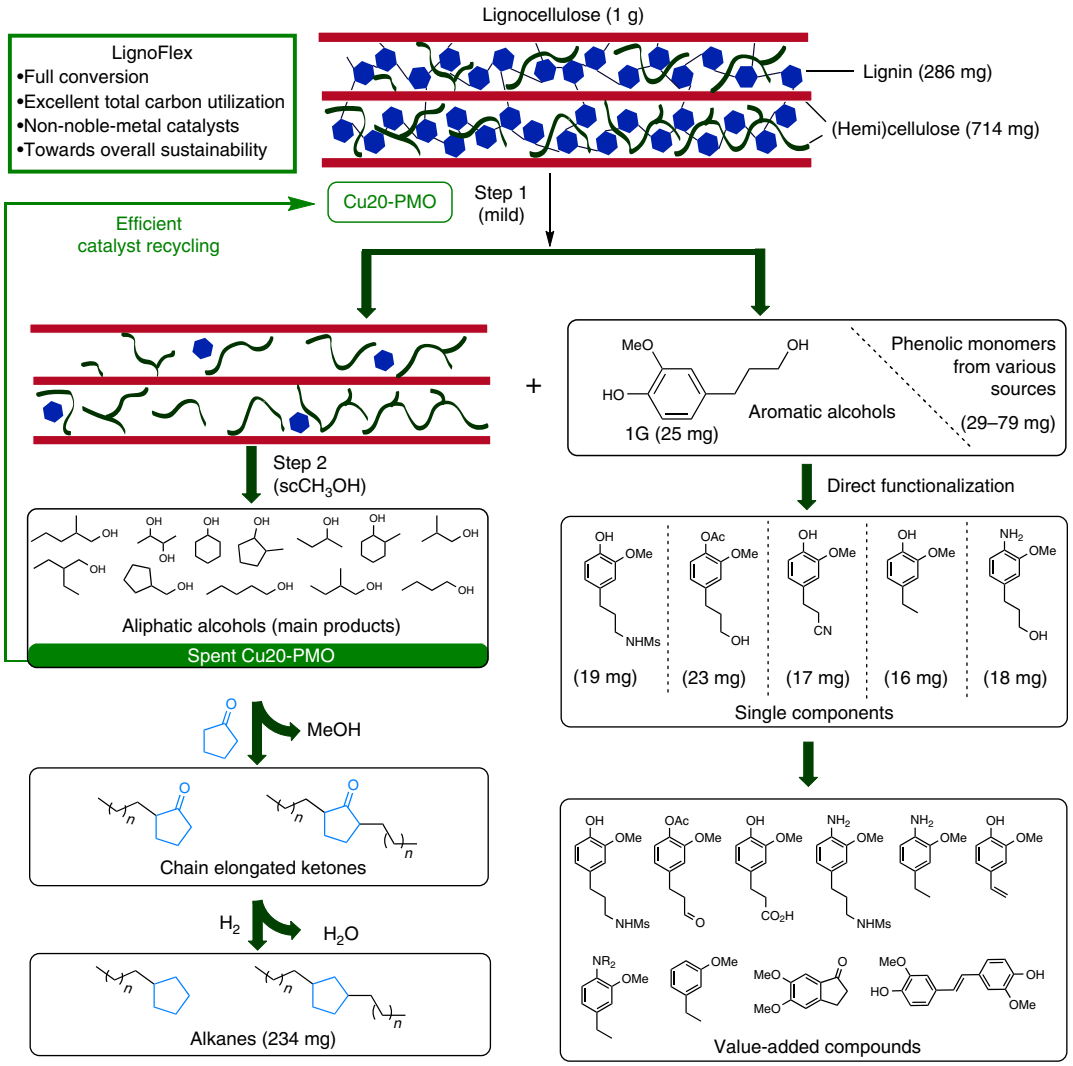


Fig. 7 | Schematic representation of the overall catalytic approach and mass balances obtained with selected pine lignocellulose. This comprehensive lignocellulose conversion strategy combines the following key aspects: (1) lignocellulose is used directly, without pretreatment and is fully converted. (2) Cu20-PMO is used in a flexible way that allows for catalyst recycling. (3) The intermediates derived from lignin and cellulose are aromatic and aliphatic alcohols, respectively, which partly retain the inherent complexity of the renewable starting material. Further catalytic pathways take advantage of this functionality to produce value-added products. (4) Products from cellulose are shown on the left-hand side: convergent pathways from mixtures of alcohols to alkanes. (5) Products from lignin are shown on the right-hand side: divergent functionalization pathways of **1G** (lignin-derived platform chemical) to high-value products. $scCH_3OH$, supercritical methanol.

Several breakthroughs have previously been achieved[40–42] regarding the use of aromatic monomers obtained on reductive lignin depolymerization for polymer applications such as epoxy thermosets, polycarbonates and cyanate ester resins (see also Supplementary Note 13).

Similarly, specific compounds obtained here could serve as starting materials for existing or emerging diverse bio-based polymers (Fig. 8a, Supplementary Note 13)[42,43]. Firstly, some of the compounds synthetized here have already found applications as polymer building blocks. For instance, compound **7** was used to synthesize a series of well-defined bio-based poly(vinylguaiacols) with phenolic functions[44]. **6** is a building block for the synthesis of epoxy resins, polyesters or polyurethanes[42,43]. Stilbene (**7S**) serves as starting material for bisphenol-A analogues[42], while **3G** and **6** can also be used as precursors for synthesis of sustainable bisphenols[42,43].

Secondly, besides existing applications, the building blocks described here will open new avenues toward the development of new, emerging renewable polymeric materials as potential replacements for petroleum-derived plastics (Supplementary Note 14)[42,43]. Compound **7** may serve as a building block in various glycopolymers used for drug or gene delivery systems[45]. Due to the similar structure to vanillin alcohol, **1G** can also be used for synthesis of bisphenols, epoxy resins, polyesters or polyurethanes[43]. Building blocks **1G**, **4**, **5**, **6**, **12a–c** and **13** can potentially serve as precursors for new polyesters or polyamides as sole components or by co-condensation with bio-derived diols or dicarboxylic acids[43]. On catalytic demethylation, **5** is an attractive monomer for the synthesis of advanced biomimetic glues[46].

The functionalized aromatics may also be used for the synthesis of pharmaceutically relevant compounds (Fig. 8b and Supplementary Note 13). For example, **1G** can be used for the synthesis of XH-14, a widely used pharmaceutically active compound for the treatment of coronary heart disease[47]. Compound **6Cy** from acid **6** can be turned into anti-Alzheimer's donepezil by using commercially available reagents[48]. **12b** can be used as intermediate in the synthesis of carbazole derivatives[49]. Furthermore, amines **9a–9e**

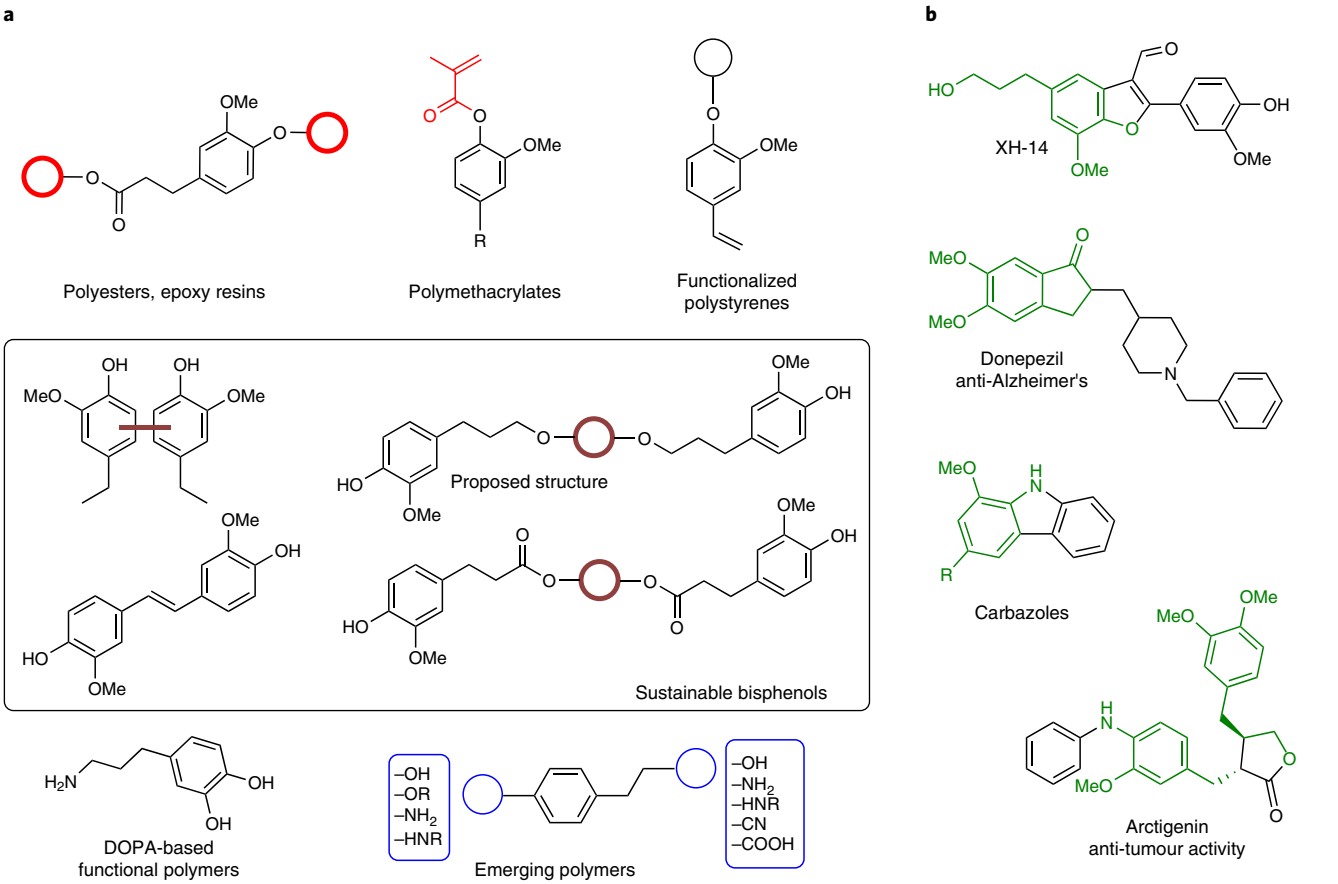


Fig. 8 | Potential applications of compounds obtained from 1G. a, Applications of the building blocks obtained in the synthesis of polymers. **b**, Proposed applications of the lignin-derived building blocks as pharmaceutical intermediates. The fields in green show moieties obtained from lignin. More details on the existing and potential applications of the building blocks obtained can be found in Supplementary Notes 13 and 14.

are structural motifs in synthetic arctigenin derivatives that show anti-tumour properties[50]. Lignin-derived pharma intermediates represent low-volume and high-value products and demonstrate the prospect of constructing pharmaceutically active compounds from lignin in a few reaction steps, greatly reducing the amount of waste produced.

Conclusions

The catalytic strategies developed here derive substantial value from both the lignin as well as the cellulose components of lignocellulosic biomass. The overall approach embraces the complexity of the renewable starting material and provides aromatic and aliphatic alcohol intermediates for further direct transformations. This small 'model biorefinery' (Fig. 7) provides access to a range of products with concrete valorization potential (Fig. 8). We have shown that aromatic alcohol **1G**, isolated as a single component, can serve as a lignin-derived platform chemical as it was obtained in high selectivity and converted to higher-value building blocks including amines. Notably, among these transformations is the direct coupling of **1G** with ammonia. Furthermore, we found that the unique reactivity of the noble-metal-free catalyst (Cu20-PMO) used in the first, mild depolymerization step, enables the conversion of process residues that would otherwise block the catalyst to aliphatic small molecules, thereby enabling catalyst recycling. Gratifyingly, the subsequent catalytic upgrading of the complex aliphatic alcohol mixtures to alkanes via chain elongation and hydrogeoxygenation was achieved using non-noble-metal catalysts.

During the course of designing new catalytic steps along the reaction network, it became apparent that reactivity is largely influenced by the inherent structure of the renewable building blocks, in many cases resulting in improved reactivity, in some cases presenting limitations to methodology development. This will serve as motivation for catalysis reasearch, for example to accomplish the direct catalytic coupling of ammonia with lignin-derived phenols or methoxy-aromatics. Globally, the approach described herein will inspire the development of fully sustainable biorefineries.

Methods

Preparation of Cu20-PMO. The catalyst prepared in this procedure is a porous metal oxide, denoted as Cu20-PMO, which indicates that in a 3:1 Mg/Al hydrotalcite precursor 20% of the Mg^{2+} ions were replaced with Cu^{2+} ions. The hydrotalcite (HTC) catalyst precursor was prepared by co-precipitation. In a typical procedure, a solution containing $AlCl_3{\cdot}6H_2O$ (12.07 g, 0.05 mol), $Cu(NO_3)_2{\cdot}2.5H_2O$ (6.98 g, 0.03 mol) and $MgCl_2{\cdot}6H_2O$ (24.40 g, 0.12 mol) in deionized water (0.2 l) was added to a solution containing Na_2CO_3 (5.30 g, 0.05 mol) in water (0.3 l) at 60 °C under vigorous stirring. The pH was kept between 9 and 10 by addition of small portions of a 1 M solution of NaOH. The mixture was vigorously stirred at 60 °C for 72 h. After cooling to room temperature, the light-blue solid was filtered and re-suspended in a 2 M solution of Na_2CO_3 (0.3 l) and stirred for overnight at 40 °C. The solids were filtered and washed with deionized water until chloride free. After drying the solid for 6 h at 100 °C, 15.07 g of the HTC was obtained. Before use, 4 g of HTC was calcined at 460 °C for 24 h in air and to yield 2.5 g of Cu20-PMO catalyst.

Mild depolymerization of lignocellulose. Typically, the autoclave was charged with 0.2 g Cu20-PMO catalyst, 1 g of lignocellulose, 20 mg of 3,5-dimethylphenol (internal standard) and 10 ml of methanol. The reactor was sealed and pressurized with 40 bar H_2 at room temperature. The reactor was heated to 180 °C for a predetermined amount of time, and stirred at 400 r.p.m. and subsequently cooled to room temperature. Then, 0.1 ml solution was collected with a syringe and injected to GC-MS and GC-FID after filtration with a PTFE filter (0.42 µm). After, the contents of the reactor (solution and solids) were transferred to a 50 ml centrifuge

tube by washing with additional methanol. The methanol soluble fraction was separated from the solids by centrifugation and subsequent decantation. The solid was additionally washed with methanol (2 × 40 ml) and dried overnight in the desiccator under vacuum until constant weight. The combined methanol solution was collected in a round bottom flask and the solvent was removed. The weight of the residue (methanol soluble products) was determined. **1G** was isolated from pine lignocellulose by column chromatography on silica gel with pentane:ethyl acetate (4:1) as eluent.

Conversion of methanol insoluble residues in supercritical methanol. The solid residue obtained after the mild depolymerization reactions described above was further treated according to the following procedure. The solid residues containing unreacted lignocellulose mixed with the Cu20-PMO catalyst were placed in 10 ml Swagelok stainless steel microreactors. Typically, the lignocellulose solids originating from conversion of 1 g lignocellulose were first separated to four equal parts based on weight and then transferred to four identical microreactors. 3 ml methanol was then added to each reactor and they were sealed and placed into an aluminum block preheated to 320 °C. After the indicated reaction time, the microreactors were rapidly cooled in an ice-water bath and the contents of the reactors were quantitatively transferred to a centrifuge tube. The liquids were separated by centrifugation and decantation and subsequently analysed by GC-MS-FID. The remaining solids were dried in a desiccator under vacuum overnight until stable weight.

Data availability. All data are available from the corresponding author upon reasonable request.

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Author contributions

K.B. conceived the idea, supervised the research and wrote the manuscript. Z.S. designed the LignoFlex process and performed all related chemical reactions. Z.S. also performed reactions related to Stage 2 and synthesized compounds **3G**, **4** and **6**. G.B. and A.A. contributed equally to this research and designed pathways for the functionalization of **1G** and synthesized compounds **5**, **7**, **7S**, **8**, **9a–e**, **10**, **11**, **12a–c**, **13**, **14** and **15**. M.C.A.S. performed catalyst characterization. P.J.D. measured and analysed the 2D-HSQC NMR data and was involved in figure preparation. B.F. contributed to the catalytic conversion of alcohol mixture to alkanes, and designed synthetic pathways to obtain compound **6Cy**. All of the authors commented on the manuscript during its preparation.

Competing interests

The authors declare no competing financial interests.

Additional information

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